Remarks/Arguments:

Claims 1-30 were pending in the application at the time of the Office Action. New claim 31 is added herewith, reciting a step of washing the surface to remove unbound fluorophore. Support may be found in the sentence spanning pages 12 and 13 of the application. Claims 23-30 are withdrawn as directed to an nonelected invention, and claims 4, 8-13, 15, 17, 18, and 21 are withdrawn as directed to nonelected species. Applicants submit that the designation of claim 18 as nonelected is incorrect, and appears to result from a misunderstanding due to examiner having read the original version of certain passages in the application that were subsequently amended. Specifically, as amended in Applicants' response of March 8, 2007, page 18 at line 31 now refers to the reactive moiety being product 5 in Fig. 2. Thus, the DTNB becomes part of the reactive moiety, not part of the fluorophore. Rather, as shown in Fig. 2, the nitrobenzoic moiety is displaced by the fluorophore to form product 6. Also see the amended text in the paragraph beginning at page 9, line 7. The fluorophore mentioned there is indeed that recited in claim 7. Accordingly, Applicants submit that claim 18 recites elected species and should be examined. However, pending further consideration by the examiner on this point, the status of claim 18 is annotated herein as "Withdrawn - Previously Presented."

35 U.S.C. § 112

Claim 4 is rejected under 35 U.S.C. § 112, 1st paragraph for lack of support for the term "divalent aromatic," and requires cancellation of that term. Claim 4 is amended herewith accordingly, and Applicants submit that the rejection has now been overcome.

Claims 1-3, 5-7, 14, 16, 19, 20 and 22 are rejected under 35 U.S.C. § 112, 2nd paragraph as indefinite for leaving out essential steps. The examiner refers to claim 1 as reciting cleaving the linking bond immediately after it is formed. Applicants respectfully point out that claim 1 does not require that the cleaving be done immediately, and notes that there may be intervening steps because the method comprises the listed steps. Additional steps, for example washing the surface to remove unbound fluorophore, may also be included. See the sentence bridging pages 12 and 13. However, removal of unbound fluorophore is not always required. For example, the method can work even if a substantial amount of fluorophore is irreversibly adsorbed on (but not reacted with) the surface. See page 13 at lines 23-26. In any case, the linking bond is eventually cleaved to liberate the fluorescent moiety for analysis, and this step satisfies the examiner's request that there be "One or more steps directed to doing something with the formed 'linking bond'." For these reasons, Applicants submit that claim 1 and its dependents are not indefinite, and respectfully request withdrawal of the rejection.

Claim 5 is rejected for being indefinite with respect to the orientation of "-SH" with respect to fluorescein in compounds "Fl-SH." Applicants amend claim 5 herewith to remove reference to "Fl-SH," and submit that the rejection has now been overcome. No new matter has been added.

35 U.S.C. § 103

Claims 1-3, 5-7, 14, 16, 19 and 20 are rejected under 35 U.S.C. § 103(a) as unpatentable over Pope and Knigge (US 5,399,501) in view of Melancon (US 4,922,113).

The examiner points to the 6th sentence of the Abstract of Pope and Knigge to purportedly disclose a method of determining a binding capacity of a surface. The examiner asserts that a diagnostic binding assay is a determination of the binding capacity of a surface. This assertion is in error. Binding assays have nothing to do with determining the binding capacity of a surface, but rather with measuring the amount of an analyte in a fluid sample.

> "Binding assays have found widespread application in the field of clinical diagnostics for the detection and/or measurement of drugs, hormones, proteins, peptides, metabolites, microorganisms and other substances of interest, commonly referred to as analytes, in both biological and non-biological fluids." (Column 1, lines 23-28, emphasis added)

Applicants note that the Abstract, and in fact the whole patent, is concerned with providing immobilized (i.e., bound) specific binding members on a surface, to use as a tool in detecting and quantifying analytes in fluid samples. Pope and Knigge do not disclose quantifying (by any means, with or without fluorescence) a moiety that is liberated from a surface to calculate the binding capacity of that surface as presently claimed. In fact, Pope and Knigge do not calculate the binding capacity of a surface at all. Thus, this claim element is entirely missing.

The examiner points to column 7, line 50, which discloses using N,N'-didansyl-L-cystine as a coupling agent. As noted throughout the application, Pope and Knigge use coupling agents to immobilize (bind) specific binding members to a surface. See Abstract, claim 1, et al. For instance, Example 19 uses N,N'-didansyl-L-cystine to immobilize a specific binding member (HIV-1 gp41) on a surface (amino-microparticles). The N,N'-didansyl-L-cystine is first bound to the microparticles, and then reductively cleaved with dithiothreitol to form thiolated microparticles to which the specific binding member is eventually attached. While it may be true that the reductive cleavage liberates N-dansyl-L-cysteine (a fluorophore) from the surface of the microparticles, the supernatant containing the liberated N-dansyl-L-cysteine is discarded.

Column 15, lines 52-53. No quantification of this liberated fluorophore is performed. It is a waste product. Even the other half of the original N,N'-didansyl-L-cystine molecule, now in the form of an N-dansyl-L-cysteine moiety attached to the microparticle surface, is not quantified. Rather, it merely functions to subsequently immobilize the specific binding member (HIV-1 gp41) on the microparticles. As noted in the Abstract, it is the immobilized specific binding member, not N-dansyl-L-cysteine moieties, that may be used for diagnostic binding assays, i.e., the quantification of analytes in fluid samples. No surface binding capacities are ever determined, by any means.

Pope and Knigge teach nothing whatsoever about quantifying coupling agents such as N,N'-didansyl-L-cystine. Rather, it is the specific binding members that may be attached to the surface by such coupling agents that are of interest to Pope and Knigge.

> "The general methodology of the present invention involves the modification of a solid phase by the introduction of thiol groups. A specific binding member, e.g., a protein antigen, is also modified to contain thiol-reactive functional moieties such as maleimides or active halogens. The derivatized specific binding member is then added to the thiolated solid phase and reacted to produce a covalent linkage." (Column 8, lines 50-57)

There is no disclosure in Pope and Knigge of quantifying any species, including fluorescent ones, that are liberated from a surface by cleaving a linking bond or group. Nor do Pope and Knigge determine a binding capacity of a surface. These claim elements are entirely missing.

Melancon does not remedy this deficiency. Melancon teaches using fluorescence measurements to monitor the weight or thickness of coatings such as adhesives, primers, release coatings, etc. See paragraph beginning at Column 2, line 55. Typical substrates for the coatings "...include any solid surface, for example, those of paper, cardboard, wood, cork, plastic ...". See Column 4, lines 18-19. Melancon measures the fluorescence of a fluorophore that is bound to the surface. The examiner asserts that it would have been obvious to apply this technique to the methods of Pope and Knigge, but it is difficult to see why. Melancon is looking for coating irregularities; Pope and Knigge don't even use coatings. Melancon's surfaces are large surfaces; Pope and Knigge's are microparticles. Melancon quantifies certain aspects of the surface; Pope and Knigge use their invention to quantify analytes in a fluid sample.

Nonetheless, even if Melancon's techniques were somehow applied to Pope and Knigge's microparticles, this would still entail measuring the fluorescence of bound, not liberated, fluorophores as claimed. Therefore, this claim element is not taught by the combination of Pope and Knigge and Melancon, which combination is therefore deficient as a basis for *prima facie* obviousness.

Claim 22 is rejected under 35 U.S.C. § 103(a) as unpatentable over Pope and Knigge and Melancon as applied to claims 1, 2 and 20, and further in view of Burns et al., 56 J. Org. Chem. 2648 (1991). Burns is relied upon to disclose the use of tris(2-carboxyethyl)phosphine as a reducing agent. However, Burns does not remedy the aforementioned deficiencies of the Pope and Knigge and Melancon references. Accordingly, not all claim elements have been provided by the combined references, and a *prima facie* case of obviousness has not been presented. Therefore, the rejection should be withdrawn.

Conclusion

Applicants submit that the application is now in condition for allowance, and respectfully request reconsideration and notification of same. Applicants invite the examiner to contact their undersigned representative, Frank Tise, if it appears that this may expedite examination.

Respectfully submitted,

Frank P. Tise

Christopher A. Rothe Reg. No. 54,650
Frank P. Tise Reg. No. 50,379
Attorney and Agent for Applicants

CAR/FPT/gdb

Attachments:

Dated: March 13, 2008

RatnerPrestia
P.O. Box 1596
Wilmington, DE 19899
(302) 778-2500

The Director is hereby authorized to charge or credit Deposit Account No. **18-0350** for any additional fees, or any underpayment or credit for overpayment in connection herewith.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, with sufficient postage, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on: **March 13, 2008.**

Jeffrey E. Mitchell